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Original Research

Can the halp score, a new prognostic tool, predict the progression of pseudoexfoliation patients to pseudoexfoliation glaucoma?

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Abstract

Aim: The present study aims to investigate the prognostic role of hemoglobin, albumin, lymphocyte, and platelet (HALP) score in pseudoexfoliation syndrome (PEXS) patients and its relationship with pseudoexfoliation glaucoma (PEXG) progression.

Material and Methods: This retrospective study included 58 PEXS and 61 PEXG patients. All groups ' demographic information and hemograms, s were collected from the hospital automation system. The neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), systemic immuno-inflammatory index (SII), systemic inflammatory response index (SIRI), pan-immune inflammation value (PIV), and HALP were calculated to both groups. The results were compared among the groups.

Results: In this study, there were 119 participants in total: 58 patients with PEXS with an average age of 71.3 ± 8.9 years and 61 patients with PEXG with an average age of 71.3 ± 8.9 years (p=0.15). In paired comparisons, it was observed that the NLR, PLR, SII, SIRI, and PIV indices of the groups were not found to be statistically significant (p>0.001). The HALP score value was lower in the PEXG group than the PEXS (4.73 ±1.99 and 6.3 ±2.63, respectively) (p<0.001). The AUC of the HALP score for PEXS and PEXG was 0.696. The optimal cut-off value of HALP to predict PEXG was ≤ 4.23, with 85% sensitivity and 51.7% specificity (95% confidence interval 0,605-0,777, p<0.01).

Discussion: It was found that a lower HALP score was significantly associated with PEXG patients and could be an independent prognostic factor. Although this score alone is not sufficient, this study is important in that it may predict the possibility of developing PEXG.

Keywords

Halp Score, Pseudoexfoliation Glaucoma, Pseudoexfoliation Syndrome

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Introduction

Pseudoexfoliation syndrome (PEXS) is an age-related systemic disease affecting the extracellular matrix. It is characterized by the overproduction and accumulation of extracellular elastic fibrillary substance (pseudoexfoliation), particularly in the anterior segment of the eye [1]. The prevalence of PEXS increases with age and varies among countries. For instance, the prevalence of PEXS in individuals over the age of 60 is 25% in Iceland, 20% in Finland, 6.3% in Norway, 4.7% in Germany, 4% in England, and 0% in the Eskimo population, whereas it has been reported as 5-11.2% in Turkey [2- 4]. PEXS is strongly associated with elevated intraocular pressures in up to 44% of patients, leading to the subsequent development of pseudoexfoliation glaucoma (PEXG). It is recognized as the most commonly identified cause of secondary open-angle glaucoma [5]. In Turkey, the prevalence of PEXG patients was 26.8% in individuals over 60 years old [4].

The pathophysiology of PEXS and pseudoexfoliation glaucoma (PEXG) patients have been associated with systemic and ocular inflammation. In the literature, it has been reported that the values of many cytokines and chemokines are high in PEXS/PEXG patients in aqueous humor and serum [6- 8]. Tumor necrosis factor-alpha (TNF-α) and high sensitivity C-reactive protein (hs-CRP) levels, which are considered to be markers of inflammation and peripheral endothelial dysfunction, were also measured to be high in patients with pseudoexfoliation [9]. Recently, increased inflammatory biomarkers calculated by hemogram parameters have been a research topic in ocular inflammation diseases such as PEXS, dry eye disease, and glaucoma [10- 13]. Neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) inflammatory indexes were observed to be significantly higher in PEXS and PEXG patients than healthy group [12]. In a study evaluating another inflammatory index marker, the systemic immuno-inflammatory index (SII), it was found that there was an association between higher SII with PEXS and PEXG [14]. These studies suggested that PLR, NLR, and SII may be useful in predicting the prognosis of PEXS patients and progression to PEXG.

The hemoglobin, albumin, lymphocyte, platelet (HALP) score consisting of complete blood count parameters and albumin has been defined as a new inflammatory index. In recent studies, the HALP score has been proven to be a good prognostic indicator in patients such as malignancy and acute ischemic stroke [15- 18]. This inflammatory index has not been previously evaluated in PEXS and PEXG patients associated with systemic inflammation. According to our knowledge, our study is the first to evaluate the association of HALP score with PEXS prognosis and progression to PEXG. Our study aims to investigate the prognostic role of HALP score in PEXS patients and its relationship with PEXG progression.

Material and Methods

A total of 119 patients, of which 61 had PEXG and 58 had PEXS, were diagnosed between March 2022-2023 at Aksaray University Training and Research Hospital's Ophthalmology Department and were subsequently followed up. Demographic information for both the study and control groups was retrieved from the hospital automation system. The study was approved by the local ethics committee following the Declaration of Helsinki principles, and all participants gave informed written consent.

Patients with PEXS exhibited normal optic nerve head results, a standard visual field, and intraocular pressure (IOP) less than 21 mm Hg, in addition to the characteristic pseudoexfoliative material deposition observed during dilated eye examinations. In contrast, the PEXG group exhibited pseudoexfoliative material, along with evidence of IOP> 21 mm Hg, glaucomatous optic neuropathy, and glaucomatous damage in the visual field. Exclusion criteria encompassed autoimmune disorders, cardiac diseases, diabetes mellitus, hyperlipidemia, hypertension, acute systemic infections, ocular conditions other than pseudoexfoliation and cataract, recent surgery within the last 3 months, malignancy history, ongoing systemic medications affecting blood parameters (especially steroids), and a history of smoking or alcohol consumption.

The NLR, PLR, SII, systemic inflammatory response index (SIRI), pan-immune inflammation value (PIV), and HALP, respectively, were calculated as follows:

neutrophils ÷lymphocytes

platelets ÷lymphocytes

platelets ×(neutrophils ÷lymphocytes)

(neutrophils ×monocyte)÷lymphocytes

(neutrophils×platelets ×monocytes)÷lymphocytes

(hemoglobins ×albumins ×lymphocytes)÷platelets

Statistical Analyses

The study groups underwent statistical analysis using version 22 of the Statistical Package for the Social Sciences (SPSS). The Kolmogorov-Smirnov test was employed to assess the normality of the data. A t-test was used for comparing continuous variables, presenting results in means and standard deviations. In cases where variables deviated from a normal distribution, the Mann-Whitney U test was utilized for comparison. Statistical significance was determined at a threshold of $p<0.05$. Receiver operating characteristic curves (ROCs) were created to address the predictive role of HALP.

Ethical Approval

This study was approved by the Ethics Committee of Aksaray University (Date: 2023-06-22, No: 70-SBKAEK).

Results

A total of 119 patients -58 with PEXS and 61 with PEXG- with average ages of 71.3 ± 8.9 years and 71.3 ± 8.9 years, respectively, participated in this study. There were no gender or age-related statistically significant differences between the groups (Table 1). The median and minimum-maximum results of the hemogram parameters, albumin, and inflammatory indexes among both groups are presented in Table 2.

There was no statistically significant distinction between the hemogram parameters and albumin levels of the groups ($p>0.05$). Furthermore, inflammatory indices for the PEXS and PEXG groups were computed. In paired comparisons, it was detected that the NLR, PLR, SII, SIRI, and PIV indices of the groups were not found to be statistically significant ($p>0.001$, Table 2). The HALP score value was lower in the PEXG group than in the PEXS (4.73 ±1.99 and 6.3 ±2.63, respectively) ($p<0.001$) (Table 2). The AUC of the HALP score for PEXS and

Table 1. Demographic information of the study groups

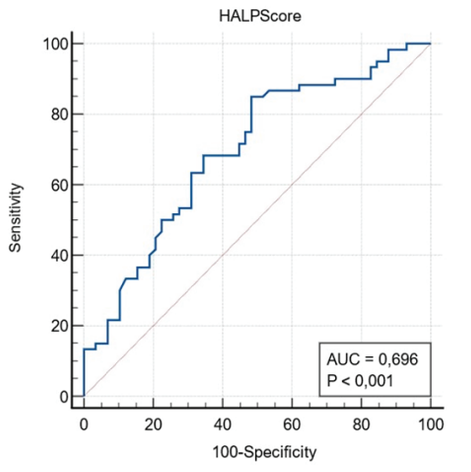
Parameters		PEXS (n=58) Mean ± SD	PEXG (n=61) Mean ± SD	p
Gender	Male	24 (41%)	37 (61%)	0.11*
	Female	34 (59%)	24 (39%)	
Age (year)		72.5 ± 8.4	75.3 ± 8.6	0.156¥

*Chi-Square test ¥ Student t-test

Table 2. Comparison of the blood parameters of the PEXS and PEXG groups

Parameters	PEXS (n=58) median (min-max)	PEXG (n=61) median (min-max)	p*
White Blood Cell (103µL)	7.05 (3.24-10.77)	7.9 (2.25-17.43)	0.108
Neutrophil (103µL)	4.42 (2.09-7.8)	5.25 (0.91-14.28)	0.059
Lymphocyte (103µL)	1.9 (0.63-3.88)	2.15 (0.67-4.47)	0.044
Monocyte (103µL)	0.46 (0.21-0.84)	0.52 (0.11-1.06)	0.031
Hemoglobin (g/dL)	13.42 (9-18.2)	13.75 (9.4-17.5)	0.297
Platelet (103µL)	231.5 (115-330)	218.3 (104-401)	0.102
MPV (fL)	10 (7.8-13.9)	10.1 (8-12.6)	0.676
Albumin (g/L)	40.6 (29.3-48.5)	41.23 (27.6-49)	0.369
SII	597 (213-1700)	603 (140-3454)	0.649
SIRI	1.26 (0.24-4.81)	1.47 (0.2-5.88)	0.149
PIV	284.4 (64.6-867.1)	323.9 (16.4-1934)	0.306
NLR	2.63 (0.78-6.41)	2.57 (0.8-10.5)	0.794
PLR	133.4 (56.1-274.6)	116.5 (3-250.9)	0.045
HALP	6.3 (2.03-15.5)	4.73 (1.26-9.1)	<0.001

*Mann- Whitney U test NLR: Neutrophil Lymphocyte Ratio, CRP: C-reactive protein, MPV: Mean Platelet Volume, PLR: Platelet Lymphocyte ratio, dNLR: Derived NLR ratio (neutrophil count divided by the result of WBC count minus neutrophil count), SII: Systemic inflammatory index (neutrophil x platelet/ lymphocyte count), SIRI: Systemic inflammatory response index (neutrophil × monocyte/lymphocyte count), PIV: Pan-immune inflammation value (neutrophil × platelet × monocyte /lymphocyte count), and HALP: hemoglobin, albumin, lymphocyte, platelet (hemoglobin × albümin × lymphocyte/platelet count)



Variable	Cut-off	AUC	95%CI	Sens	Spec	P value
HALP Score	≤4,23	0,696	0,605-0,777	51,72	85	<0,0001

Figure 1. ROC curve of HALP for discrimination between PEXS (n = 58) and PEXG (n = 61).
HALP, hemoglobin albumin lymphocyte platelet; PEXS, pseudoexfoliation syndrome; PEXG, pseudoexfoliation glaucoma, ROC, receiver operator characteristic.

PEXG was 0.696. The optimal cut-off value of HALP to predict PEXG was ≤ 4.23, with 85% sensitivity and 51.7% specificity (95% confidence interval 0,605-0,777, p<0.01) (Figure 1).

Discussion

This is the first study to examine hemogram and albumin parameters and novel inflammatory indices, including NLR, PLR, SII, SIRI, PIV, and HALP scores together in patients with PEXS and PEXG. In the present study, no significant difference was detected among PEXS and PEXG patients in NLR, PLR, SII, SIRI, and PIV indexes. However, our findings provided evidence for the association between HALP score and PEXG. According to ROC analysis, a cut-off value of 4.23 for HALP was determined to distinguish between PEXS and PEXG. This is the first study, as far as we are aware, to investigate the value of the HALP score to predict the PEXG prognosis of PEXS patients.

In recently, several studies have demonstrated that parameters easily calculated from hemograms are valuable in showing the role of inflammation in some ocular diseases [10, 11, 19, 20]. Among PEX-related inflammatory index studies, Ozgonul et al. detected that NLR and PLR were high in PEX patients and that a high NLR could predict PEXS and PEXG [12]. In the study of Tukenmez Dikmen et al., it was stated that the PEXS group had the highest NLR and SII values, followed by the PEXG and control groups, and there was no difference in PLR values between the groups [14]. In another study, Mirza et al. compared the monocyte count/high-density lipoprotein ratio (MHR) and lymphocyte/monocyte ratio (LMR) indexes in PEX and control groups.

Moreover, it was detected that MHR was higher and LMR was lower in the PEX group than in the healthy group [21]. In the present study, the results of PEXS and PEXG were compared to research the prognostic role of inflammatory indexes in both patients. Although NLR, SII, SIRI, and PIV values were relatively higher in PEXG patients than in PEXS patients, this difference was not found to be statistically significant between the groups. Current studies have shown that the HALP score can reflect the inflammation condition of patients and has been proven to be an important prognostic indicator for patients with especially tumors [18, 22]. Studies have shown that the HALP score can be evaluated as a negative predictive biomarker for the prognosis of the disease [22, 23]. A meta-analysis, which included a total of 28 studies with 13,038 patients, revealed that pre-treatment, a low HALP score was a dependable and prognostic indicator for survival results in cancer patients [22]. Another study conducted by Bayram et al. reported that the HALP score was lower in severe hyperemesis gravidarum and was significantly different from mild hyperemesis gravidarum. According to the hypothesis of the authors, the HALP score can be a practical, affordable, and easily accessible objective biomarker to predict the existence and severity of hyperemesis gravidarum [23]. In the present study, our findings indicate that the HALP score was significantly lower in patients with PEXG compared to the PEXS patients. PEXS has a strong association with high intraocular pressures in up to 44% of patients, and this situation subsequently leads to the development of PEXG [5]. Therefore, our study indicates that the HALP score can be a negative predictive biomarker in the development of PEXG.

In the meantime, we demonstrated that the cut-off value for the HALP score in the ROC curve analysis was 4.23. We hypothesized that the risk of developing PEXG may be higher in PEXS patients below this value.

As far as we are aware, this is the first study to analyze the prognostic significance of the HALP score in patients with PEX. The strength of this study is the use of systemic inflammation biomarkers and HALP score, which are prognosis indicators together to investigate the progression to PEXG.

Limitation

There are some limitations in our study. First, the study is conducted in a single-center setting. Second, this study population is comparatively small.

Conclusion

In conclusion, in our study comparing PEXS and PEXG patients, the inflammatory biomarkers NLR, PLR, SII, SIRI, and PIV and the new biological indicator HALP score were studied together. It was found that a lower HALP score was significantly associated with PEXG patients and could be an independent prognostic factor. Although this score alone is not sufficient, this study is important in that it may predict the possibility of developing PEXG. Larger-scale prospective studies should investigate and validate these predictive inflammatory biomarkers in patients with PEXS and PEXG.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or compareable ethical standards.

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Conflict of Interest

The authors declare that there is no conflict of interest.

References

1. Schlotzer-Schrehardt U, Naumann GO. Ocular and systemic pseudoexfoliation syndrome. Am J Ophthalmol. 2006;141(5):921-37.

2. Forsius H. Prevalence of pseudoexfoliation of the lens in Finns, Lapps, Icelanders, Eskimos, and Russians. Trans Ophthalmol Soc UK. (1962). 1979;99(2):296-8.

3. Yalaz M, Othman I, Nas K, Eroglu A, Homurlu D, Cikintas Z, et al. The frequency of pseudoexfoliation syndrome in the eastern Mediterranean area of Turkey. Acta Ophthalmol (Copenh). 1992;70(2):209-13.

4. Yildirim N, Yasar E, Gursoy H, Colak E. Prevalence of pseudoexfoliation syndrome and its association with ocular and systemic diseases in Eskisehir, Turkey. Int J Ophthalmol. 2017;10(1):128-34.

5. Jeng SM, Karger RA, Hodge DO, Burke JP, Johnson DH, Good MS. The risk of glaucoma in pseudoexfoliation syndrome. J Glaucoma. 2007;16(1):117-21.

6. Yildirim Z, Yildirim F, Ucgun NI, Sepici-Dincel A. The role of the cytokines in the pathogenesis of pseudoexfoliation syndrome. Int J Ophthalmol. 2013;6(1):50-3.

7. Okutucu M, Arpa M. Evaluation of serum semaphorin 3A and interleukin 6 levels in patients with pseudoexfoliation syndrome. Int Ophthalmol. 2023;43(6):1995-2002.

8. Garweg JG, Zandi S, Pfister IB, Skowronska M, Gerhardt C. Comparison of cytokine profiles in the aqueous humor of eyes with pseudoexfoliation syndrome and glaucoma. PLoS One. 2017;12(8):e0182571.

9. Sorkhabi R, Ghorbanihaghjo A, Ahoor M, Nahaei M, Rashtchizadeh N. High-sensitivity C-reactive protein and tumor necrosis factor-alpha in pseudoexfoliation syndrome. Oman Med J. 2013;28(1):16-9.

10. Ozarslan Ozcan D, Kurtul BE, Ozcan SC, Elbeyli A. Increased systemic immune-inflammation index levels in patients with dry eye disease. Ocul Immunol Inflamm. 2022;30(3):588-92.

11. Tang B, Li S, Han J, Cao W, Sun X. Associations between blood cell profiles and primary open-angle glaucoma: A retrospective case-control study. Ophthalmic Res. 2020;63(4):413-22.

12. Ozgonul C, Sertoglu E, Mumcuoglu T, Ozge G, Gokce G. Prediction of pseudoexfoliation syndrome and pseudoexfoliation glaucoma by using neutrophil to lymphocyte ratio and platelet to lymphocyte ratio. Ocul Immunol Inflamm. 2016;24(6):665-70.

13. Yagcı B, Erdal H. Can pan-immune inflammation value and systemic inflammatory response index be used clinically to predict inflammation in patients with cataract. ACAM.2023;14(12):1064-7.

14. Tukenmez-Dikmen N, Un Y. Systemic immuno-inflammatory index in patients with pseudoexfoliation syndrome and pseudoexfoliative glaucoma. Ther Adv Ophthalmol. 2023;(15):1–10

15. Peng D, Zhang CJ, Tang Q, Zhang L, Yang KW, Yu XT, et al. Prognostic significance of the combination of preoperative hemoglobin and albumin levels and lymphocyte and platelet counts (HALP) in patients with renal cell carcinoma after nephrectomy. BMC Urol. 2018;18(1):20.

16. Peng D, Zhang CJ, Gong YQ, Hao H, Guan B, Li XS, et al. Prognostic significance of HALP (hemoglobin, albumin, lymphocyte and platelet) in patients with bladder cancer after radical cystectomy. Sci Rep. 2018;8(1):794.

17. Chen XL, Xue L, Wang W, Chen HN, Zhang WH, Liu K, et al. Prognostic significance of the combination of preoperative hemoglobin, albumin, lymphocyte and platelet in patients with gastric carcinoma: A retrospective cohort study. Oncotarget. 2015;6(38):41370-82.

18. Tian M, Li Y, Wang X, Tian X, Pei LL, Wang X, et al. The hemoglobin, albumin, lymphocyte, and platelet (HALP) score is associated with poor outcome of acute ischemic stroke. Front Neurol. 2020;(11):610318.

19. Elbeyli A, Kurtul BE, Ozcan SC, Ozarslan Ozcan D. The diagnostic value of systemic immune-inflammation index in diabetic macular oedema. Clin Exp Optom. 2022;105(8):831-5.

20. Elbeyli A, Kurtul BE. Systemic immune-inflammation index, neutrophil-to-lymphocyte ratio, and platelet-to-lymphocyte ratio levels are associated with keratoconus. Indian J Ophthalmol. 2021;69(7):1725-9.

21. Mirza E, Oltulu R, Katipoglu Z, Mirza GD, Ozkagnici A. Monocyte/HDL ratio and Lymphocyte/Monocyte ratio in patients with pseudoexfoliation syndrome. Ocul Immunol Inflamm. 2020;28(1):142-6.

22. Xu H, Zheng X, Ai J, Yang L. Hemoglobin, albumin, lymphocyte, and platelet (HALP) score and cancer prognosis: A systematic review and meta-analysis of 13,110 patients. Int Immunopharmacol. 2023;(114):109496.

23. Bayram F, Ozgen G, Karasin SS, Ozgen L. The predictive value of HALP score and systemic immune inflammation (SII) index in hyperemesis gravidarum. J Obstet Gynaecol Res. 2023;49(7):1729-35.

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